

**What is claimed is:**

1. A method of analyzing tissue, the method comprising:  
illuminating a tissue with coherent or partially coherent light;  
receiving light reflected from the tissue at a detector to form a series of speckle patterns; and  
analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue.
2. The method of claim 1, wherein the microscopic motion is Brownian motion.
3. The method of claim 1, wherein the microscopic motion is motion of cells or cellular organelles.
4. The method of claim 1, further comprising compensating for macroscopic motion to isolate the microscopic motion.
5. The method of claim 1, wherein the tissue is *in vivo*.
6. The method of claim 1, wherein the tissue is internal tissue.
7. The method of claim 6, wherein the illuminating step comprises providing an invasive device coupled to a light source, passing the device into a patient, placing the device in proximity to the tissue, and shining coherent or partially coherent light from the light source onto the tissue.
8. The method of claim 7, wherein the invasive device is selected from the group consisting of a catheter, an endoscope, and a laparoscope.
9. The method of claim 7, wherein the placing step includes placing the device in direct contact with the tissue.
10. The method of claim 1, wherein the coherent light comprises laser light.

11. The method of claim 1, wherein the partially coherent light comprises light from a superluminescent diode.

12. The method of claim 1, wherein the detector is located farther than one wavelength of light from the tissue and detects far field speckle.

13. The method of claim 1, wherein the detector is located within one wavelength of light from the tissue and detects near field speckle.

14. The method of claim 1, wherein the analyzing step comprises comparing each of the series of speckle patterns to a series of reference speckle patterns, and quantifying the temporal correlation differences between the speckle patterns and the reference patterns.

15. The method of claim 14, wherein the analyzing step comprises digitizing each of the speckle patterns, and the quantifying step comprises evaluating a cross-correlation between the speckle patterns and the reference patterns.

16. The method of claim 14, wherein the analyzing step comprises digitizing each of the speckle patterns, and the quantifying step comprises evaluating a maximum cross-correlation between the speckle patterns and the reference patterns.

17. The method of claim 15, wherein the analyzing step further comprises determining a decorrelation rate for the speckle patterns.

18. The method of claim 1, wherein the analyzing step further comprises analyzing spatial characteristics of the speckle pattern to deduce structural characteristics of the tissue.

19. The method of claim 1, wherein the analyzing step further comprises analyzing spatial characteristics of the speckle pattern to deduce biomechanical characteristics of the tissue.

20. The method of claim 18, wherein the illuminating step comprises illuminating multiple locations of the tissue in succession, the receiving step comprises forming a separate series of speckle patterns for each respective section of the tissue, and the analyzing step comprises analyzing each separate series of speckle patterns and comparing the separate series to deduce structural differences between the respective locations of the tissue.

21. The method of claim 4, wherein compensating for macroscopic motion comprises performing the receiving step during a diastole of a heartbeat.

22. The method of claim 4, wherein macroscopic motion comprises patient motion.

23. The method of claim 4, wherein the macroscopic motion is peristalsis.

24. The method of claim 4, wherein receiving comprises gathering reflected light at a light receptor and transmitting the gathered light to the detector, and wherein compensating for macroscopic motion includes coupling the receptor to the tissue.

25. The method of claim 4, wherein compensating for macroscopic motion includes excluding changes in the speckle patterns caused by non-random motion during the analysis step.

26. The method of claim 4, wherein macroscopic motion results from blood flow between the tissue and the reflector, and the compensating step comprises replacing the blood with a transparent solution.

27. The method of claim 1, wherein the tissue comprises an atherosclerotic plaque

28. The method of claim 1, wherein the tissue comprises a tumor, a tumor margin, necrotic tissue, ischemic tissue, or damaged tissue.

29. A method of determining the susceptibility to rupture of an atherosclerotic plaque having a lipid pool and a fibrous cap, the method comprising:

- illuminating the plaque with coherent or partially coherent light;
- receiving light reflected from the plaque at a detector to form a series of speckle patterns;
- gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the lipid pool; and
- assessing the plaque's vulnerability to rupture from the amount of microscopic motion.

30. The method of claim 29, further comprising analyzing spatial characteristics of the speckle pattern data to deduce structural characteristics of the plaque.

31. The method of claim 30, wherein analyzing comprises assessing the thickness of the fibrous cap.

32. The method of claim 31, wherein cap thickness is assessed by

- (i) measuring the decorrelation time constant  $\tau$  as a function of  $r = (x_0^2 + y_0^2)^{1/2}$ ;
- (ii) measuring optical properties of the cap; and
- (iii) comparing the measured optical properties and  $\tau(r)$  to a mathematical simulation that models light remittance as a function of cap layer thickness.

33. The method of claim 32, wherein the optical properties are measured by computing first and second order statistics of a speckle probability distribution function or by using diffuse reflectance spectrophotometry.

34. The method of claim 32, wherein the mathematical simulation is a Monte Carlo simulation or diffusion theory simulation.

35. The method of claim 31, wherein a plaque is considered vulnerable to rupture if the thickness of the fibrous cap is less than about 60 microns.

36. The method of claim 30, wherein analyzing comprises assessing the viscosity of the lipid pool.

37. The method of claim 36, wherein the plaque is considered vulnerable to rupture if the viscosity of the lipid pool has a time constant of less than about 200 milliseconds.

38. The method of claim 36, wherein the plaque is considered likely to rupture if the viscosity of the lipid pool has a time constant of less than about 100 milliseconds.

39. A method of analyzing a tissue structure, the method comprising:  
illuminating the tissue structure with coherent or partially coherent light;  
receiving light reflected from the tissue structure at a detector to form a series of speckle patterns;  
gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue; and  
assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure.

40. The method of claim 39, wherein analyzing comprises assessing the thickness of the tissue structure.

41. The method of claim 40, wherein tissue structure thickness is assessed by  
(i) measuring the decorrelation time constant  $\tau$  as a function of  $r = (x_0^2 + y_0^2)^{1/2}$ ;  
(ii) measuring optical properties of the tissue structure; and  
(iii) comparing the measured optical properties and  $\tau(r)$  to a mathematical simulation that models light remittance as a function of tissue structure thickness.

42. The method of claim 41, wherein the optical properties are measured by computing first and second order statistics of a speckle probability distribution function or by using diffuse reflectance spectrophotometry.

43. The method of claim 41, wherein the mathematical simulation is a Monte Carlo simulation or diffusion theory simulation.

44. A method of detecting a vulnerable atherosclerotic plaque having a lipid pool and a fibrous cap within a blood vessel, the method comprising:

illuminating a segment of the blood vessel *in vivo* with coherent or partially coherent light;

receiving light reflected from the interior vessel wall of the segment at a detector to form a series of speckle patterns;

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the interior vessel wall; and

comparing speckle pattern time constants to a known speckle pattern time constant for a normal blood vessel and a known speckle pattern time constant for an atherosclerotic plaque;

wherein speckle pattern time data corresponding to a speckle pattern time constant for an atherosclerotic plaque indicates the segment of the blood vessel contains a vulnerable atherosclerotic plaque.

45. The method of claim 44, further comprising analyzing spatial characteristics of the speckle pattern data to determine structural characteristics of the plaque.

46. The method of claim 45, wherein analyzing comprises assessing the thickness of the fibrous cap.

47. The method of claim 46, wherein a plaque is considered vulnerable to rupture if the thickness of the fibrous cap is less than about 60 microns.

48. The method of claim 46, wherein analyzing comprises assessing the viscosity of the lipid pool.

49. The method of claim 45, wherein the plaque is considered vulnerable to rupture if the viscosity of the lipid pool has a time constant of less than about 200 milliseconds.

50. The method of claim 49, wherein the plaque is considered likely to rupture if the viscosity of the lipid pool has a time constant of less than about 100 milliseconds.

51. A fiber optic probe for detecting speckle patterns in a sample, the probe comprising

a catheter including a rotatable inner shaft and a transparent outer sheath;

a fiber array housed within the shaft and comprising one or more first optical fibers for transmitting incident light to the sample and one or more second optical fibers for transmitting light remitted from the sample; and

a mirror arranged near a distal end of the shaft to reflect light passing through the fiber array onto a sample outside the transparent outer sheath and back from the sample through the fiber array.

52. The fiber optic probe of claim 51, wherein the shaft can rotate 360 degrees within the sheath.

53. The fiber optic probe of claim 51, wherein the fiber array comprises a single first optical fiber for transmitting incident light to the sample.

54. The fiber optic probe of claim 51, wherein the fiber array comprises multiple first optical fibers for transmitting incident light to the sample.

55. The fiber optic probe of claim 51, wherein the fiber array comprises a single second optical fiber for transmitting light remitted from the sample.

56. The fiber optic probe of claim 51, wherein the one or more fibers selected to transmit incident light are the same as the one or more fibers selected to transmit remitted light.

57. The fiber optic probe of claim 51, wherein one fiber of the array is selected as the first optical fiber to transmit incident light to the sample, and thereafter a different fiber is

selected as the first optical fiber to transmit incident light to the sample, thereby scanning light across the sample.

58. The fiber optic probe of claim 51, further comprising an inflatable balloon connected to the sheath.

59. An optical system for detecting speckle patterns in a sample, the system comprising

a fiber optic probe of claim 51;  
a coherent or partially light source connected to an optical fiber within the fiber array;  
a detector to receive light remitted from the sample; and  
a processor to process the remitted light and to analyze speckle patterns remitted from the sample.

60. The system of claim 59, wherein the processor comprises a reference speckle pattern.

61. The system of claim 59, wherein the processor comprises an analog-digital converter to convert the analog remitted light into a digital signal.